REMARKS

Claim status

Claims 1 and 11 are amended herein.

Claims 12, 22-23, and 31 have been cancelled herein without prejudice or disclaimer.

No new matter has been added by these amendments.

Claim rejections

35 U.S.C. § 112

Claims 1-14 and 19-31 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. In particular, the Office Action states that "since the claim does not recite how much of dTTP was present, it cannot be determined how much dUTP constitutes a 10-50% replacement of the dTTP which was originally present." OA, at p. 4. Claims 1 and 11 have been amended to recite that the combined amount of dTTP and dUTP in the reaction mixture is generally equivalent to the concentration of the other conventional nucleotides, and that the dUTP may comprise about 10% to about 100% of the amount of dTTP. The recitation captures combinations of dTTP and dUTP ranging from a ratio of about 9:1 (e.g., wherein dUTP replaces about 10% of dTTP) to 1:1 (e.g., wherein dUTP replaces about 50% of dTTP). Support for this amendment may be found in the specification as filed, *see, e.g.*, ¶¶ [0012], [0059] and Example 1, ¶¶ [0077]-[0081]. Applicants respectfully assert that an ordinarily skilled artisan would be able to readily determine the relative amount of dTTP and dUTP in the invention as presently claimed. Accordingly, the rejection on this basis is rendered moot and Applicants respectfully request withdrawal of the same.

35 U.S.C. §§ 102, 103

Claims 1, 2, 3, 7-12, 24, 25, and 27-31 were rejected under 35 U.S.C. § 102 as allegedly anticipated by U.S. Patent No. 5,731,171 (hereinafter "Bohlander"). Claims 1-3. 5, 7-12, 24, 25, and 27-31 are rejected under 35 U.S.C. §102 as allegedly anticipated by U.S. Patent Publication No. 2003/0073081 (hereinafter "Mukai"). Further, claims 1-12 are rejected under 35 U.S.C. §103 as allegedly obvious over Mukai in view of U.S. Patent No. 6,783,940 (hereinafter "McLaughlin"). In particular, it is stated that Bohlander discloses a reagent composition comprising "each of dATP, dCTP, dGTP, and dTTP . . . in combination with 40 μM

Bio-11-dUTP," and that Mukai discloses "'0.625 mM each of dATP, dCTP, and dGTP, 0.625 mM of a dTTP+Aminoallyl dUTP mixture,'" and thus that each individually anticipate the reaction mixture of claim 1. OA, at pp. 5-6 (emphasis added).

Applicants respectfully disagree. Firstly, both Bohlander and Mukai disclose the use of a conjugated dUTP, e.g., Bio-11-dUTP or Aminoallyl-dUTP, for purposes other than reducing primer aggregation. The present claims, in contrast, are limited to the nucleotide deoxyuridine triphosphate (dUTP). In particular, Bohlander teaches only the use of dUTP functionalized with a detectable label, e.g., Bio-11 or Spectrum-Orange. (*Bohlander*, at Col. 16, lines 17-26; Col. 20, lines 46-67), while Mukai describes the use of dUTP functionalized with aminoallyl. (*Mukai*, at paragraphs [0954] and [0958]). The presently-claimed invention does not encompass such conjugated molecules as functionalization of the dUTP as described in these references would likely obviate the very effect the present invention seeks to achieve by including dUTP in the reaction mixture, *i.e.*, reduction of primer aggregation. Accordingly, neither reference can properly anticipate the invention as presently claimed.

Secondly, Claims 1 and 11 have also been amended to clarify that the respective reaction mixture and method as claimed lack a uracil-degrading enzyme and an enzyme degradation step to degrade uracil containing amplicons. Support for this amendment may be found in the application as filed, see, e.g., originally filed claim 12. As indicated in the specification, dUTP has typically been employed in conjunction with an enzyme that degrades uracil as a general method for reducing contamination, wherein the dUTP will typically completely replace the dTTP in the amplification mixture. (*See, Specification*, at ¶ [0008]. In contrast, the present invention is directed toward substituting dTTP in a reaction mixture with dUTP to reduce primer aggregation, and as such, does not require degradation of uracil containing amplicons.

In this regard, Mukai specifically teaches that "[i]n the detection method of the present invention, dUTP may be incorporated as a substrate during amplification of a target nucleic acid. Thus, if dUTP is used as a substrate, it is possible to prevent carry-over contamination of amplification products utilizing uracil N-glycosidasase." (*See, Mukai*, at ¶ [0404]). Accordingly, with respect to non-functionalized dUTP Mukai merely discloses its conventional use in conjunction with a uracil degrading enzyme (e.g., UDG, UNG, endoribonuclease, etc.) to reduce contamination, and clearly does not teach or suggest a combination of dTTP and dUTP in reaction mixtures for amplification wherein the reaction mixture and the amplification method

lack a uracil degrading enzyme. (*See, e.g., Specification*, ¶ [0008]). Bohlander also fails to provide any such teaching or motivation to modify their reaction mixtures to arrive at the instant invention. Accordingly, neither of these references can render obvious the invention as presently claimed, whether taken alone or in combination.

Moreover, Applicants also note that Mukai is directed toward isothermal amplification reactions in which the reaction mixtures remain at 60° C. In contrast, new claim 31 requires an amplifying step comprising heating the target nucleic acid to a temperature greater than 60° C as described and exemplified throughout the specification. (*See, e.g., Specification*, ¶ [0048]).

Having distinguished the independent claims from the art of record, Applicants respectfuly submit that the claims dependent therefrom are patentable for at least the same reasons. However, Applicants reserve the right to separately address the patentability of the dependent claims in the future, should that be necessary. Reconsideration and withdrawal of the rejections is respectfully requested.

CONCLUSION

Applicants respectfully submit that the instant application is in condition for allowance. Entry of the amendments and an action passing this case to issue is therefore respectfully requested. Should there be any remaining issues that remain unresolved, the Examiner is encouraged to telephone the undersigned at (415) 356-3064.

Respectfully submitted,
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